OPEN ACCESS

ORIGINAL ARTICLE

Accuracy of Mentzer index for predicting iron deficiency anemia in adults

Farhan Aslam[1], Savida Ilyas Dar[2], Sarah Azam Shah[3], Muhammad Aqeel[4], Abdur Rehman[5] and Lubna Meraj[6]

[1, 2, 3] Department of General Medicine, Federal Government Poly Clinic Hospital, Islamabad, Pakistan,
[4] Department of General Medicine, Pakistan Institute of Medical Sciences, Islamabad Pakistan,
[5] Department of General Medicine, Rawalpindi Medical University, Rawalpindi Pakistan,
[6] Department of General Medicine, Benazir Bhutto Hospital, Rawalpindi Medical University, Rawalpindi, Pakistan.

ABSTRACT

Background: It is of great clinical significance to differentiate between causes of microcytic, hypo chromatic anemias, iron deficiency anemia being one of them as it will improve with iron supplements. Complete blood picture is unable to differentiate. Iron studies and Hemoglobin electrophoresis are expensive tests. This necessitates the need of a cost-effective test and therefore we tried to determine the effectiveness of mentzer index in predicting iron deficiency anemia.

Methods: It was an Observational, Cross-sectional study, conducted in Department of General Medicine, Federal government polyclinic hospital, Islamabad. Patients with microcytic hypochromic anemia, both from indoor and outdoor were included in study. Iron deficiency Anemia was diagnosed by iron studies (serum ferritin, Serum Iron, TIBC and transferrin saturation) and then mentzer index was calculated to check accuracy. Patient with normocytic or macrocytic anemia or other cell lines deficiency, patients with infectious diseases or inflammatory process were excluded from study.

Results: A total of 155 patients were included in the study. Out of all the patients 145(93.5%) had mentzer index of > 13 while 10(6.5%) had mentzer index of <13. All of 150 patients (100%) had transferrin saturation lessthan 20 % indicating iron deficiency anemia against 93.5% picked up by Mentzer index. The receiver operator curves (ROC) showed that the MCV was the most important predictor of anemia while calculating mentzer index. The AUC value for MCV was 0.886(CI: 95%, 0.806-0.966, p value <0.000). MCV value between 52.6 to 63.5 fl predicted that the Mentzer index would be above 13, thus suggesting iron deficiency anemia with a sensitivity of more than 86%.

Conclusion: Study findings support the use of Mentzer index, particularly MCV, as a valuable tool for predicting iron deficiency anemia.

Keywords: Mentzer index, Mean corpuscular volume (MCV), Red blood cells (RBC).

This article may be cited as: Aslam F, Ilyas Dar S, Azam Shah S, Aqeel M, Rehman A, Meraj L. Accuracy of Mentzer index for predicting iron deficiency anemia in adults Int J Pathol; 22(3): 149-155. https://doi.org/10.59736/IJP.22.03.916

Introduction

Iron deficiency anemia (IDA) is a widespread public health concern particularly in developing countries including Pakistan. Iron deficiency anemia is the most common cause of anemia worldwide (1). It indicates limited or abnormal red blood cells with decreased capacities to meet the body's oxygen (2). According to WHO estimates in 2004, Iron Deficiency Anemia accounted for 273,000 cases of mortality, 97% happening in middle- and low-income countries (3).

CORRESPONDENCE AUTHOR
Farhan Aslam
Department of General Medicine, Federal Government Poly Clinic Hospital, Islamabad, Pakistan
Email: fa0975791@gmail.com

In Pakistan, the prevalence of Iron deficiency anemia is 70-80% in pregnant patients (4). Differentials of microcytic, hypochromic anemia have immense clinical significance as each has its unique treatment plan and prognosis (5). Iron supplements can benefit in Iron Deficiency Anemia but unnecessary in beta-thalassemia trait; whilst both have similar clinical symptoms i.e. shortness of breath and fatigue (6). Thus, it is of utmost significance to discriminate between the two. Complete blood picture is unable to differentiate, whereas Iron studies and Hemoglobin electrophoresis are costly tests thus this necessitate the need of a cost-effective screening test which is widely available. Although there are many indices available, the most convenient in our setup is Mentzer Index, calculated as ratio of mean corpuscular volume (MCV) to red cell count (RBC), indicated as MCV (fl)/RBC count (millions per microliter). Index >13 indicate Iron deficiency anemia, while a value <13 can be a likely indicator of Beta thalassemia (7).

The purpose of this study was to determine the diagnostic accuracy of Mentzer Index to predict Iron Deficiency Anemia. Iron Studies (Serum ferritin, Serum Iron, TIBC and transferrin saturation) were used as gold standard to diagnose Iron Deficiency Anemia. Mentzer index was then calculated and compared. This may help us derive a cost-effective solution to effectively diagnose our patients, keeping in mind the regional socioeconomic factors.

Methods

The observational study was conducted in department of Medicine, Federal government polyclinic (FGPC) Hospital Islamabad for a period of 6 months after approval from ethical board via letter number FGPC.1. /12/2020 dated 15th Nov 2022. Sample Size was calculated by using sensitivity and specificity calculator and was found to be 115 with confidence level of 95%, specificity 83%, prevalence 41% and Absolute precision 9%. Patients with hemoglobin of less than 11 (HB <11) of Microcytic hypochromic type, from indoor as well as outdoor were included in study. Iron deficiency Anemia was diagnosed by iron studies (serum ferritin, Serum Iron, TIBC and transferrin saturation) and then Mentzer index was calculated to check accuracy. Patient with normocytic anemia, macrocytic anemia, patients with other cell lines deficiency, those with infectious diseases or inflammatory process were excluded from study. The normal values for serum iron: 50-70 Microgram/dl, TIBC 250-450 and Ferritin10-291 ng/ml were taken as reference values for diagnosing iron deficiency anemia. Data was analyzed using SPSS version 23.

Results

A total of 155 patients were included in the study. The base line demographics of

patients included in the study are given in the Table 1, describing the mean age, mean Hemoglobin, MCV, RBC count and the Mean Corpuscular Hemoglobin Concentration (MCHC). It also gives an account of the distribution of the different parameters among the study participants.

Table 1: Baseline characteristics of the study population (150)

Variables		Mean ± SD
Age (Years)		41.55±18.84
MCV (femtoliters)		68.57±6.42
Hematocrit (%)		27.48±5.25
Red Blood Cell (million cells per microliter)		3.95±2.84
MCHC (grams per deciliter)		29.56±3.63
MCH (picograms)		22.80±11.21
White Blood Cell (cells per microliter)		7305.63±2476.38
Retics (%)		1.32±0.98
Serum Ferritin (nanograms per milliliter)		6.50±3.32
Serum Iron (micrograms per deciliter)		20.74±10.15
Total Iron Binding Capacity (micrograms per deciliter)		390.99±86.42
Mean Hemoglobin (9g/dl)		7.68±1.85
Peripheral film	Microcytosis, Hypochromia, Anisocytosis, Target Cells, Pencil Cells	65(41.9%)
	Microcytosis, Hyperchromasia	84(54.2%)
	Anisocytosis	5(3.2%)
	Target Cells	1(0.6%)
Hemoglobin	less than 7	61(39.4%)
	7 to 9	47(30.3%)
	9 to 11	47(30.3%)
Platelets	<150,000	3(1.9%)
	150000-450000	124(80.0%)
	More than 450000	28(18.1%)
Transferrin saturation	<20 % >20-50%	155(100%)

Table 2 gives an overview of the different characteristics alongside their P values in both the groups based on Mentzer index. Those having Mentzer index > 13 had mean MCV of 69.19±6.05 as compared to 59.55±4.80 (p <0.000) in the group with Mentzer index < 13. RBC count in Mentzer index> 13 was 3.87±0.63 as compared to 5.11±0.70 in the group with Mentzer index < 13. (p <0.000).

Table 2: Comparison of demographic and hematological parameters by Mentzer Index Status

Variables		Mentzer Index		p-value
		> 13	< 13	
Age		41.93±18.97	36.00±16.82	0.338
MCV		69.19±6.05	59.55±4.80	0.000*
Hematocrit		27.24±5.21	31.04±4.69	0.027*
RedBlood cell		3.87±0.63	5.11 ±0.70	0.000*
MCHC		29.72±3.62	27.22±3.13	0.035*
MCH		22.92±11.38	21.02±8.57	0.857
White Blood Cell		7238.53±2410.87	8947.0±2025.02	0.030*
Retics		1.33±1.0	1.26±0.57	0.82

serum Ferritin		6.43±3.30	7.39±3.61	0.383
Serum Iron		20.54±10.12	23.60±10.75	0.350
Total Iron Binding Capacity		393.08±86.03	360.70±99.90	0.25
Hemoglobin (g/dl)		7.66±1.88	8.00±1.54	0.569
Gender	Male	45(31%)	3(30%)	0.940
	Female	100(69%)	7(70%)	
Hemoglobin	less than 7	59(40.7%)	2(20%)	0.106
	7 to 9	41(28.3%)	6(60%)	
	9 to 11	45(31%)	2(20%)	
Peripheral film	Microcytosis, Hypochromasia, Anisocytosis, Target cells, pencil cells	60(41.4%)	5(50%)	0.893
	Microcytosis, Hypochromasia	79(54.5. %)	5(50%)	
	Anisocytosis	5(3.4%)	-	
	Target cells	1(0.7%)	-	
Platelets	<150,000	3(2.1%)		0.892
	150000-450000	116(80%)	8(80%)	
	More than 450000	26(17.9%)	2(20%)	

*p<0.05 is considered statistically significant

Table 3: Mentzer index, Transferrin saturation and Anemia on Hemoglobin levels

	Hb <7g/dl	Hb7-9g/dl	Hb 9-11 g/dl	Total
Mentzer index > 13	59 (38.1%)	41 (26.5%)	45 (29%)	145(93.5%)
Mentzer index < 13	2 (1.3%)	6 (3.9%)	2 (1.3%)	10 (6.5%)
Transferrin saturation<20%	61 (39.4%)	47 (30.3%)	47 (30.3%)	155 (100%)

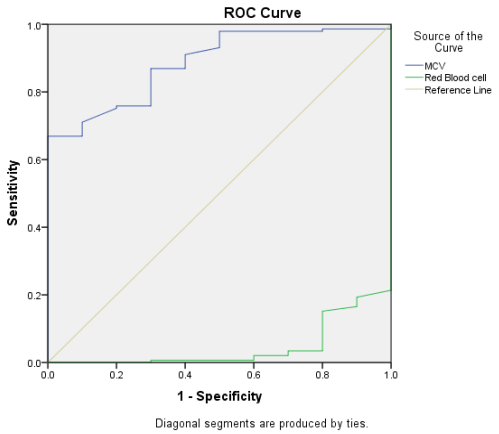
Table 3 shows that out of 155 anemic patients 145(93.5%) had a Mentzer index of > 13 while only 10(6.5%) had Mentzer index of <13. All the patients who underwent the study had transferrin saturation less than 20 % making it as a 100 % sensitive tool to pick iron deficiency anemia. Mentzer index could pick up iron deficiency anemia in 93.5% of the patients against 100 percent picked up by transferrin saturation.

The receiver operator curves were obtained for the different components for calculating the Mentzer index and its accuracy in terms of detection of anemia.

It showed that the Mean corpuscular volume (MCV) was the most important predictor of anemia in terms of mentzer index. The AUC value for MCV was 0.886 (CI: 95%, 0.806-0.966, p value <0.000). An MCV value between 52.6 to 63.5 fl predicted that the Mentzer index would be above 13, thus suggesting iron deficiency anemia.

Table 4: Area under the Curve (AUC)

Test Result Variable(s)	Area	Std. Error	p-value	95% Confidence Interval	
				Lower Bound	Upper Bound
MCV	.886	.041	.000	.806	.966
Red Blood cell	.044	.024	.000	.000	.091



Mentzer index achieved an impressive predictive accuracy of 93.5% among patients of iron deficiency anemia, as defined by transferrin saturation levels in the study. This index, calculated by dividing the mean corpuscular volume (MCV) by the red blood cell (RBC) count, serves as a crucial diagnostic tool in differentiating IDA from other types of anemia. Furthermore, the MCV alone demonstrates a high sensitivity of over 88.6% in predicting whether the Mentzer index will exceed 13, thereby highlighting its utility in early identification of IDA. This relationship underscores the importance of RBC indices in clinical settings, as they provide a straightforward and effective means for clinicians to assess and manage anemia types, ultimately improving patient outcomes through timely intervention.

Discussion

Anemia is defined as low red cell mass with decreased oxygen carrying capacity and it has several causes. Iron deficiency anemia is the most common anemia out of all in developing countries (8). It is usually diagnosed by using specific markers like ferritin, serum transferrin saturation (calculated using the iron levels and the total iron binding capacity) and other less specific tools like erythrocyte indices of which Mentzer index has been used the most.

Our study was designed to evaluate the effectiveness of mentzer index in predicting iron deficiency anemia in patients. The results show a significant association between mentzer index and iron deficiency anemia, with 93.5% of patients having mentzer index greater than 13. This finding is compatible with previous studies done by Sharma et al (9) and Abdul Husain et al (10) that demonstrated 96% patients and 100% (48/76) patients had Mentzer index of >13 respectively. The mean corpuscular volume (MCV) was found to be most important predictor of anemia, with AUC value of 0.886. Additionally, the mean MCV value in our study was 69.19±6.05 fl in patients with a Mentzer index above 13, indicating iron deficiency anemia. This is in line with research by Korom et al (11) and Salam Al kindi et al in Oman (12) highlighting the importance of MCV in diagnosing iron deficiency anemia in which it was from 72 till <80 fl.

In our study we found that a Mentzer index greater than 13 can predict iron deficiency anemia with high accuracy of 93.5%. These findings support the use of the Mentzer index as a valuable tool in diagnosing iron deficiency anemia, particularly in resource-limited settings where more advanced diagnostic tests may not be available as suggested by Balci et al (13) in Turkey, Jacob Ransom et al in Nigeria (14), Heya shah et al in India (15) (95.6% sensitivity) and Atika Sherali et al in Pakistan in children (sensitivity of 82.3% while specificity of 98.7%) respectively (16).

Overall, our study demonstrates the effectiveness of the Mentzer index in predicting iron deficiency anemia. The ability to accurately identify patients at risk of iron deficiency anemia will allows for timely interventions, which can improve patient

outcome. The study's results also have implications for resource allocation and healthcare planning. By identifying patients at risk of iron deficiency anemia, healthcare providers can target interventions and resources more effectively, reducing the burdens on health care systems and ameliorating health outcome.

Conclusion

Our study findings support the use of Mentzer index, particularly MCV, as a valuable tool for predicting iron deficiency anemia. The results may have important implications for clinical practice, healthcare planning and resources allocation. However, there is need of further research to confirm the findings and explore the effectiveness of Mentzer index in different populations.

Conflict of interest: None.
Funding: No funding was received for this project

References

1. Wawer AA, Jennings A, Fairweather-Tait SJ. Iron status in the elderly: A review of recent evidence. Mech Ageing Dev. 2018 Oct; 175:55-73. Doi: 10.1016/j.mad.2018.07.003.
2. Habib A, Kureishy S, Soofi S, Hussain I, Rizvi A, Ahmed I, et al. Prevalence and Risk Factors for Iron Deficiency Anemia among Children under Five and Women of Reproductive Age in Pakistan: Findings from the National Nutrition Survey 2018. Nutrients. 2023 Jul 28; 15(15):3361. doi: 10.3390/nu15153361.
3. Ali SA, Abbasi Z, Shahid B, Moin G, Hambidge KM, Krebs NF,et al. Prevalence and determinants of anemia among women of reproductive age in Thatta Pakistan: Findings from a cross-sectional study. PLoS One. 2020 Sep 24; 15(9):e0239320. Doi: 10.1371/journal.pone.0239320.
4. Zulqarnain H, Nadeem MT, Shahid H, Mujtaba A, Ikram F, Arshad Z. Validity of Mentzer Index in Predicting Iron Deficiency Anaemia. Pak Armed Forces Med J 2024; 74(1): 63-66.DOI: https://doi.org/10.51253/pafmj.v74i1.
5. Idrees M, Khan JU, Riaz H, Shah MA, Shah H, Haris SM. Utilization of Mentzer Index to Discriminate Between Beta Thalassemia Minor and Anemia of Iron Deficiency, Followed by HPLC. Pakistan Journal of Medical & Health Sciences. 2023 Mar 22; 17(01):843.
6. ameel T, Baig M, Ahmed I, Hussain MB, Alkhamaly MBD. Differentiation of beta thalassemia trait from iron deficiency anemia by hematological indices. Pak J Med Sci. 2017 May-Jun; 33(3):665-669. Doi: 10.12669/pjms.333.12098.
7. Ntaios G, Chatzinikolaou A, Saouli Z, Girtovitis F, Tsapanidou M, Kaiafa G, et al . Discrimination indices as screening tests for β-thalassemic trait. Ann Hematol. 2007 Jul; 86(7):487-91. Doi: 10.1007/s00277-007-0302-x.
8. Chandrakumari AS, Sinha P, Singaravelu S, Jaikumar S. Prevalence of anemia among adolescent girls in a rural area of Tamil Nadu, India. J Family Med Prim Care. 2019 Apr; 8(4):1414-1417. Doi: 10.4103/jfmpc.jfmpc_140_19.
9. Luqman M, Wajid U, Ikhtiar F, Rashid R, Arif A, Naseem F, et al. Kausar T, Zahid A. Distribution Of ABO And Rh Blood Groups Among Type-II Diabetic Patients in Population Of Lahore, Pakistan. European chemical bulletin .13.74-82. Doi: 10.53555/ecb/2024.13.04.11

10. Mousa AO. Types of anemias with low MCV using Mentzer Index and RBC count among patients seen in Basrah Al-Sadir Teaching Hospital. Med J Babylon. 2014; 11(2):292-6.
11. Korom VG, Lueff S, Liposits A, Kellner A, Pavlovics A, Egyed M. Is iron deficiency anemia always microcytic? Pol Arch Intern Med. 2021 Feb 26; 131(2):199-201. Doi: 10.20452/pamw.15714.
12. Alkindi S, Al Musalami A, Al Wahaibi H, Althuraiya, Al S,Al Ghammari N, Panjwani V, et al. Iron deficiency and iron deficiency anemia in the adult Omani population. Journal of Applied Hematology. 2018 Jan 1; 9(1):11-5. Doi: 10.4103/joah.joah_65_17
13. Balcı T, Ayan D, Türkyürek C, Bayram E. Evaluation of diagnostic accuracy tests of erythrocyte indexes in the differential diagnosis of beta thalassemia minor and iron deficiency anemia: A preliminary report. Cukurova Medical Journal. 2021; 46(3):1009-17.
14. Jacob R, Aboko P, Eze E, Jeremiah Z. Differential diagnosis of iron deficiency anemia and beta thalassemia in Port Harcourt pregnant women using the Mentzer Index. Sanamed. 2024 Aug 9; 19(2).
15. Meraj, L, Ullah Khan, Z, Mateen, A, Bashir, S., Azeez, H, Yousuf, A, & Wajid,et al. Diabetic Peripheral Neuropathy and Impotence: A Cross-Sectional Analysis. History of Medicine, 2024 10(2), 1325-1330.
16. Sherali A, Ahad A, Tikmani SS, Sohail S. Screening of Iron Deficiency Anemia in Children Using Mentzer Index in Pakistan: A Cross Sectional Study. Glob Pediatr Health. 2023 Feb 11; 10:2333794X221130986. Doi: 10.1177/2333794X221130986.

HISTORY	
Date received:	27-09-2024
Date sent for review:	30-09-2024
Date received reviewers comments:	01-10-2024
Date received revised manuscript:	09-10-2024
Date accepted:	12-10-2024

KEY FOR CONTRIBUTION OF AUTHORS:

A. Conception/Study/Designing/Planning
B. Active Participation in Active Methodology
C. Interpretation/ Analysis and Discussion

CONTRIBUTION OF AUTHORS	
AUTHOR	**CONTRIBUTION**
Farhan Aslam	A,B,C
Savida Ilyas Dar	B,C
Sarah Azam Shah	A,B
Muhammad Aqeel	B,C
Abdur Rehman	C
Lubna Meraj	C

OPEN ACCESS

CASE REPORT

Glomus tumors in the urinary tract: a rare case and literature review

Katia Ramos Moreira Leite[1,2],Ana Carolina Armiliato Bogoevich[1], Ivan Borin Selegatto[3], Thiago José Penachim[3] and Wilmar Azal Neto[3]

[1]Faculdade de Medicina da Universidade de São Paulo,
[2]Laboratório Genoa/LPCM, [3]Universidade Estadual de Campinas – UNICAMP

ABSTRACT

Introduction: The Glomus tumor is a rare mesenchymal tumor that predominantly affects the subcutaneous skin of the distal extremities. Solid organs are rarely affected, and the urinary tract has been the reason for isolated reports. This paper reviews the occurrence of glomus tumors in the entire urinary tract.

Case Report: We report a case of a 56-year-old female, asymptomatic, with a 5.5 cm renal glomus tumor, and review the literature about the urinary tract involvement by this rare neoplasia.

Conclusion: Glomus tumor mostly behaves as a benign lesion that rarely affects solid organs, being the kidney, the most affected organ in the urinary tract. It should be considered in the differential diagnosis of another renal cell tumor, especially those that are eosinophilic.

Key words: Glomus tumor, Urinary tract, Kidney, Bladder, Immunohistochemistry

This article may be cited as: Ramos Moreira Leite K, Bogoevich ACA, Selegatto IB, Penachim TJ, Neto WA. Glomus tumors in the urinary tract: a rare case and literature review. Int J Pathol; 22(3): 156-162. https://doi.org/10.59736/IJP.22.03.891

Introduction

A glomus tumor is a perivascular mesenchymal neoplasm composed of cells from the glomus body which is a contractile neuromyoarterial structure that affects blood pressure and thermoregulation by altering cutaneous blood flow. It is part of a spectrum that includes myopericytoma, myofibroma, and angioleiomyoma. It constitutes 2% of mesenchymal tumors and affects young adults, mostly females. Although affects most frequently the skin and subcutaneous of distal extremities, particularly the nail bed, wide distribution has been described, including visceral organs as gastrointestinal tract, bone and intrathoracic region (1). The urinary tract is rarely affected, being the kidney the most frequent location, followed by bladder, testis and prostate. We report a case of a kidney glomus tumor and review the literature of the involvement of the entire urinary tract.

Case Presentation

A 56 year-old female, asymptomatic, discovered incidentally, by an abdominal ultrasound, a left renal mass measuring 5.5 cm. A computerized tomography (CT) was performed and the expansive solid, vascularized and heterogeneous lesion was observed in the upper third of the left kidney (Figure 1). The radiologic diagnosis indicated a solid renal tumor, and no biopsy was performed before surgery.

CORRESPONDENCE AUTHOR
Katia Ramos Moreira Leite
MD, PhD, Av. Angélica 2318, São Paulo, Brazil
katiaramos@usp.br

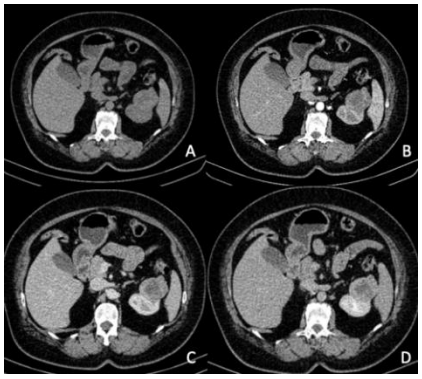


Figure 1: Computed tomography images before (A) and after intravenous injection of iodized contrast. The images show a 5.0 cm expansive lobulated, solid, vascularized, and heterogeneous lesion in the upper third of the left kidney. (B) Represents the arterial phase. The lesion exhibits greater peripheral uptake of contrast in the later stages, portal (C) and excretory (D), with hypovascularized central areas (liquefaction). Additionally, it is more than 50% exophytic and has a discreet impression in the upper calyceal group, completely above the upper polar line.

She underwent a partial left robotic assisted nephrectomy, with the use of intra operatory ultrasound, and a 5,2 cm tumor mass was resected. The surgical time was 120 minutes, the estimated blood loss was 200 ml, no drain was left in the abdomen, and the procedure was considered uneventful. Patient evolved well, and was discharged home on the first day of post-operative. She is well and an abdominal CT six months after surgery showed no sign of recurrence. This report was conducted in accordance with the Declaration of Helsinki of 1975.

Pathological Findings

The pathological analysis showed that the cut surface was uniform, brownish with no necrosis or hemorrhage. Histologically the tumor was characterized by small, epithelioid, regular, round cells, with a pale, eosinophilic cytoplasm with a round, regular, centralized nucleus. There was focal and mild atypia. The mitotic index was <1/50HPF and there were no atypical mitoses. The tumor had pushing borders and there was no necrosis, neither vascular invasion. The surgical margins were free of tumor. Immunohistochemistry study showed expression of Smooth Muscle Actin (SMA), Caldesmon (CALD), Calponin (CALP) and Vimentin (VIM). Proliferative activity (Ki67 – MIB1) was 2% (Figure 2). PAX8, Desmin, CD34, CD117, Cytokeratin 7, Cytokeratin 20, GATA3, Chromogranin, Synaptophisin were negative. The expression of Succinil-Desidrogenase B (SDHB) and Fumarate Hydratase (FH) was preserved.

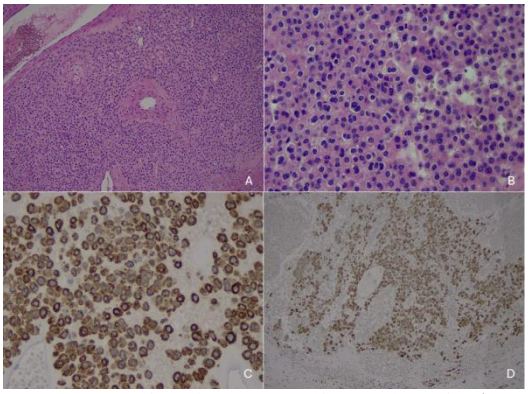


Figure 2: Routine hematoxylin and eosin (H&E) staining demonstrates a proliferation of homogenous round cells with round to ovoid nuclei arranged in multicellular layers around blood vessels. There are mild nuclear atypia and no mitoses (A) 100 × magnification; (B) 400 × magnification. Immunohistochemistry shows expression of Smooth Muscle Actin (C) and Vimentin (D). 400 x and 100 x magnification respectively.

Discussion

Glomus tumor affecting internal organs is rare, and few cases have been described in the urological tract. Kidney is the most frequently affected with 25 cases published in the literature (Table 1). It affects man twice as women, from 8 to 81 years old (mean 48.4 years old). Measures from 10 to 160 mm (mean 46.6 cm). The surgical procedure was partial or radical nephrectomy,

10 cases each. Two cases were described as inoperable, and the method of treatment was not described in 3 reports The great majority had a benign behavior and patients are described as alive and well from two to 62 months (mean 14.8 months). Three cases (12.0%) were described as malignant. Two of them inoperable and one measuring 16 cm that have recurred after a radical nephrectomy. The two patients with inoperable tumors died of the disease, six and seven months after diagnosis.

Bladder is the second urinary tract organ affected by glomus tumor (Table 2) (2-6). There are six cases published in the literature, affecting twice as men than women, with a mean age of 69.7-year-old. Gross hematuria was the main symptom. Tumor size was variable from 6.0 to 65.0 mm (mean 24.8 mm). The larger tumor showed nuclear atypia, necrosis, and high mitotic rate, and patient died from the disease 2 months after treatment. A second malignant glomus tumor was managed with radiotherapy, showing resistance to treatment, and patient died from COVID with disease 12 months after diagnosis.

There are isolated cases of glomus tumor in testicle (7, 8) both benign and one malignant glomus tumor affecting the ureter and the prostate (9, 10).

Immunohistochemistry shows consistently expression of SMA, Vimentin and type IV Collagen. CD34 positivity is variable, mostly negative. Desmin, CD31, S100, Cytokeratins, Chromogranin and Synaptophysin are negative. Genetic studies have been shown rearrangements of NOTCH genes, and BRAF (V600E) and KRAS (G12A) mutations (11).

The main differential diagnoses are myopericytoma, paraganglioma and carcinoid tumor.

Considering the kidney, the main differential diagnoses are the juxtaglomerular tumor, angiomyolipoma and eosinophilic tumors especially SDHB deficient carcinoma. Immuno-histochemistry can easily exclude angiomyolipomas (HMB45 positive) and SDHB deficient as well as other eosinophilic tumors (PAX8 and cytokeratin positives). Recently, it has been demonstrated that juxtaglomerular tumors express GATA3, serving as a useful marker to differentiate them from glomus tumors (12). GATA3 was absent in the current case.

Malignant glomus tumor are rare and the main criteria for malignancy are marked nuclear atypia, mitotic activity, the presence of atypical mitosis, deep sited tumors and size over 20 mm.

Table 1: Summary of the clinical, histological and immunoexpression aspects of the glomus tumor affecting the kidney

Ref.	Age	Sex	Presentation	Size (mm)	Nephrectomy	Atypia/ necrosis	IHC (Expression)	Mitotic activity (/50HPF)	Ki67 (%)	Follow-up mo
Our case	56	Fem	Incidental	52	Partial	Focal atypia	SMA/VIM/CALP/CALD	<1	2	NED(3)
(14)	60	Fem	Pain	110	Inoperable	Present	SMA/CIM/CALD/CALP	NA	40	DOD(7)
(15)	67	Male	Microscopic hematuria	27	NA	Absent	SMA/VIM/CD57	None	1	NED (15)
(13)	8	Male	Incidental /TSC	50	Partial	Absent	SMA/P53/RENIN	10	10	NED(16)
(16)	31	Fem	pain/ abdominal	160	Radical	Present	VIM/COLIV	NA	10	DOD (13 y) Local

			mass							recurrence
(16)	33	Fem	Abdominal mass	95	Radical	Absent	SMA/COLIV	NA	NA	NA
(16)	55	Male	Hematuria	15	Partial	Absent	SMA/CALDESMON/ COLIV	NA	NA	NED
(17)	57	Male	Abdominal disconfort	20	Partial	Absent	SMA/VIM/COLIV	2	2	NED(12)
(18)	46	Male	Incidental	NA	Radical	NA	NA	NA	NA	NA
(17)	46	Male	Incidental	50	Radical	Pleomorfism	NA	7	NA	NED(6)
(17)	66	Male	Incidental	58	Radical	Absent	SMA/GATA3	None	NA	NA
(17)	62	Male	Weight loss	18	Partial	Minimal atypia	VIM/SMA/CD57/COLIV	None	<1	NED(2)
(17)	44	Male	Back pain	Inoperable	Inoperable	pleomorfism	SMA/VIM/COLIV/ CD34	Low		DOD(6)
(17)	36	Fem	Incidental	17	Radical	Absent	SMA/VIM	None	NA	NED(8)
(17)	17	Male	Incidental	21	Partial	Absent	SMA/CALD	None	NA	NA
(17)	41	Male	Incidental	10	Partial	Absent	VIM/SMA/CD34	None	<2	NA
(17)	46	Male	Microscopic hematuria	70	Radical	Necrosis and hemorrage	SMA/VIM/CD34	3	10	NED(15)
(19)	36	Male	Abdominal tenderness	23	Partial	Focal atypia	SMA/COLIV	None	1	NED(62)
(19)	81	Male	Incidental	40	Radical	Absent	SMA/COLIV	None	NA	NED(24)
(19)	48	Male	Incidental	73	Radical	Focal atypia	SMA/COLIV	None	1	NED(33)
(17)	53	Fem	Abdominal disconfort	25	Radical	Absent	SMA/CALP/COLIV	3	10	NED(6)
(17)	55	Fem	Incidental	20	Partial	Absent	SMA/VIM	NA	NA	NA
(17)	60	Male	Incidental	25	Partial	Absent	SMA/CD34	NA	NA	NED(8)
(17)	71	Male	incidental	NA	NA	NA	NA	NA	NA	NA
(17)	34	Fem	Flank pain (pregnant)	NA	NA	NA	NA	MA	NA	NA

*DOD – Dead of the disease, NED – No evidence of disease, NA - Not available

A small subset is inherited, being described as part of Multiple Familial Glomus Tumor related to the inactivation of GLMN gene, Neurofibromatosis type 1, related to the biallelic inactivation of NF1 gene and Tuberous Sclerosis (p.Pro1315Leu) (13).

In conclusion, Glomus tumor is a rare mesenchymal tumor, affecting rarely the urinary tract, mostly the kidney, with a benign behavior in the majority of the cases. Smooth muscle antibodies, especially SMA is always positive together with Vimentin and type IV collagen. Large tumors, intense nuclear atypia, mitoses and necrosis are the main characteristics of aggressiveness.

Table 2: Summary of the clinical, histological and immunoexpression aspects of the glomus tumor affecting the bladder.

Ref.	Age	Sex	Presentation	Size (mm)	Atypia/necrosis	IHC (Expression)	Mitotic activity (/50HPF)	Ki67 (%)	Follow-up (months)
(20)	85	Male	Hematuria	NA	Atypia/necrosis	SMA/CALP	NA	60	DWD(12)
(2)	44	Male	Hematuria	16	Absent	SMA	25	5	NED (48)
(3)	57	Fem	Hematuria	6	Absent	SMA/VIM	NA	NA	NED(24)
(4)	58	Male	Incidental	25	Absent	SMA/VIM/BCL2	2		NED (12)
(5)	63	Male	Hematuria	12	Absent	SMA/CD34/IVCOL	NA	5	NED(12)
(6)	57	Fem	Hematuria	65	Atypia/necrosis/ spindle shaped cells	SMA	250	NA	DOD(2)

*DOD – Dead of the disease, DWD – Dead with the disease, NED – No evidence of disease, NA - Not available

References

1. Weissferdt A, Kalhor N, Moran CA. Intrathoracic glomus tumors and glomangiosarcomas: a clinicopathological and immunohistochemical study of 14 cases with emphasis on anatomic distribution. Virchows Arch. 2016 Nov; 469(5):541-6. Doi: 10.1007/s00428-016-2013-y.
2. Chalise S, Jha A, Neupane PR. Glomangiomyoma of Uncertain Malignant Potential in the Urinary Bladder: A Case Report. JNMA J Nepal Med Assoc. 2021; 59(239):719-22.
3. Chen L, Lai B, Su X, Wang J. Unusual glomus tumor of the bladder: a rare case report and literature review. BMC urology. 2021; 21(1):66.
4. Palmisano F, Gadda F, Spinelli MG, Maggioni M, Rocco B, Montanari E. Symplastic glomus tumor of the urinary bladder treated by robot-assisted partial cystectomy: a case report and literature review. Urologia. 2018;85(3):130-2.
5. Tripodi SA, Rocca BJ, Mourmouras V, Barbanti G, Colecchia M, Ambrosio MR. Benign glomus tumor of the urinary bladder. Archives of pathology & laboratory medicine. 2013;137(7):1005-8.
6. Shim HS, Choi YD, Cho NH. Malignant glomus tumor of the urinary bladder. Archives of pathology & laboratory medicine. 2005;129(7):940-2.
7. Tullie STE, Quraishi MK, Karawita T, Anjarwalla S. Rare presentation of a testicular glomus tumour. BMJ Case Rep. 2019;12(11).
8. Garg S, al-Talib RK, Harrison GS. Glomus tumour of the testicle. British journal of urology. 1997;80(5):823-4.
9. Sun Z, Sun F, Yu C, Xiao H, Xu Q, Gao B, et al. Malignant glomus tumor of prostate:

A case report. Frontiers in oncology. 2023;13:1121307.
10. Demir M, Tuncekin A, Yagmur I, Aydogdu A. Malignant Glomus Tumor of the Ureter. J Coll Physicians Surg Pak. 2022; 32(12):SS206-SS8.
11. Iwamura R, Komatsu K, Kusano M, Kubo C, Inaba Y, Shiba E,et al. PDGFRB and NOTCH3 Mutations are Detectable in a Wider Range of Pericytic Tumors,IncludingMyopericytomas,Angioleiomyomas, Glomus Tumors, and Their Combined Tumors. Mod Pathol. 2023 Mar; 36(3):100070. Doi: 10.1016/j.modpat.2022.100070.
12. Gupta S, Folpe AL, Torres-Mora J, Reuter VE, Zuckerman JE, Falk N, et al. Immunohistochemical expression of renin and GATA3 help distinguish juxtaglomerular cell tumors from renal glomus tumors. Hum pathol 2022 oct;128:110-23.
13. Zhao M, Yang M, Gu W, Chen X, Chen H, Kuick CH, et al. Glomus Tumor of the Kidney in a Child With Tuberous Sclerosis. Pediatr Dev Pathol. 2020;23(3):230-4.
14. Surianarayanan P, Menon AR, Sundersingh S, Raja A. Inoperable Renal Malignant Glomus Tumor, the answers for all the "W's"? J Kidney Cancer VHL. 2024;11(1):33-40.
15. Kapogiannis F, Tsiampa E. Glomus Tumor of the Kidney Harboring Malignant Potential. Cureus. 2021; 13(11):e19479.
16. Li R, Petros FG, Davis CJ Jr., Ward JF. Characterization of Glomus Tumors of the Kidney. Clin Genitourin Cancer. 2017 Sep 7:S1558-7673(17)30277-X. doi: 10.1016/j.clgc.2017.09.002.
17. Almaghrabi A, Almaghrabi N, Al-Maghrabi H. Glomangioma of the Kidney: A Rare Case of Glomus Tumor and Review of the Literature. Case Rep Pathol. 2017; 2017:7423642.
18. Lu YY, Wang RC, Wang HY. Malignant Glomus Tumor of the Kidney. Am J Med Sci. 2017;353(3):310.
19. Al-Ahmadie HA, Yilmaz A, Olgac S, Reuter VE. Glomus tumor of the kidney: a report of 3 cases involving renal parenchyma and review of the literature. Am J Surg Pathol. 2007 Apr; 31(4):585-91.
20. Ai J, Zhang S, Qian Y, Kang L, Zhang L, Zhao J. Radiotherapy and Anrotinib in Malignant Glomus Tumor of the Bladder: A Case Report and Literature Review. Cancer Biother Radiopharm. 2024;39(4):318-21.

HISTORY	
Date received:	20-5-2024
Date sent for review:	23-07-2024
Date received reviewers comments:	01-08-2024
Date received revised manuscript:	23-10-2024
Date accepted:	03-11-2024

CONTRIBUTION OF AUTHORS	
AUTHOR	CONTRIBUTION
Katia Ramos Moreirara	A,B
Wilmar Azal Neto	A,B
Ivan Borin Selegatto	C
Thiago Jose Penachim	C
Ana Carolina Armiliato Bogoevich	C

KEY FOR CONTRIBUTION OF AUTHORS:

A. Conception/Study/Designing/Planning
B. Active Participation in Active Methodology
C. Interpretation/ Analysis and Discussion